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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,216	01/15/2008	Lloyd S. Gray	1036.115US1	5782

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EXAMINER	
XIAO, YAN	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
10/06/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspto@slwip.com
request@slwip.com

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/589,216	Applicant(s) GRAY ET AL.
	Examiner YAN XIAO	Art Unit 1642

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 21 September 2011 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☐ The period for reply expires _____months from the mailing date of the final rejection.
   b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☒ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *The term "so as to induce cytostasis in said patient" raise the issue of new matter*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: ____.
   Claim(s) objected to: *7 and 10*.
   Claim(s) rejected: *7-10*.
   Claim(s) withdrawn from consideration: *1-6 and 13-15*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☒ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). See Contin. Sheet.
13. ☐ Other: _____.

/PETER J REDDIG/
Primary Examiner, Art Unit 1642

Continuation of 11. does NOT place the application in condition for allowance because:

Claim 10 remains rejected under 35 U.S.C. 103 (a) as being unpatentable over Bertolesi et al. (Mol. Pharmacol. 62:210-219, 2002, hereafter Bertolesi)) in view of Gray et al. (U. S. Patent Number 6413967, hereafter '967) for the reason of record.

The Applicant argues that Gray also fails to disclose or suggest inducing cytostasis or inducing cytostasis in a patient. As such, the Applicants assert that Gray does not remedy the deficiencies of Bertolesi.
As the 35 USC § 103 rejection of the Office Action has been obviated by the amendments to independent claim 10, claim 10 is presently believed to be in allowable condition. Reconsideration and withdrawal of the rejection of claim 10 is respectfully requested.

Applicants' arguments have been carefully considered, but have not been found persuasive because the amendment has not been entered and will not be entered for the reasons set forth above, thereforethe claims have not been amended and the rejection remains for the reasons previously set forth.

Claims 7-9 remain rejected under 35 USC 112, first paragraph, as lacking an adequate written for the reasons of record.

Applicant arges that support for claim 7 can be found in paragraph [0005] of the published application (Pub. No. 2008/0160009), which states the library of compounds that the present invention has developed can act cytostatically. In addition, paragraphs [0072] and [0073] and FIGS. 1A-1F of the present application teach that mibefradil can inhibit calcium entry in cancer cell lines. It is well known by one of skill in the art that inhibition of calcium entry can reversibly inhibit cell growth. As one of skill in the art would readily appreciate, reversible inhibition of cell growth is consistent with cytostasis rather than cytotoxicity. Such an inference would be made because preferred cytotoxic agents serve not in a reversible manner, but instead act to induce cell death. Therefore, one of skill in the art in possession of the present specification would understand that the figures and examples provided therein were aimed not at inducing cell death, but were aimed at reversible inhibition of cell growth, namely cytostasis, as presently recited in claim 7.

Applicant arges that Claims 8 and 9 are dependent upon claim 7. Accordingly, claims 8 and 9 incorporate the limitations of claim 7. As such, Applicants respectfully submit that the features of claims 7-9 are fully supported by the application as originally filed. Applicants respectfully request withdrawal of this rejection.

Applicant's arguments have been considered, but have not been found persuasive because the "cytostatically" only was meantioned once at paragraph [0005] of the Background of the Invention, only stated that the library of compuuds act cytostatically, and does not specifically point out mibefradil. The specification does not provide any guidance or examples for "inducing cytostasis" and "so as to induce cytostasis in said patient" with mibefradil. Additionally, Bertolesi teaches inhibition of T-type Ca2+ channel currents by mibefradil and provides evidences that mibefradil inhibits cell growth via cytotoxic mechanisms. See Fig. 6A, title, abstract, page 214. Thus, one of skill in the art would not predict that inhibition of cell growth by mibefradil is consistent with cytostasis rather than cytotoxicity.

Claims 7-9 are rejected under 35 USC 112, first paragraph, as failing to comply with the enablement requirement for the reasons of record.

Applicant arges that as discussed above, claim 7 currently recites, among other things, "a method for inducing cytostasis.., so as to induce cytostasis in said patient." For adequate enabling support the Applicants point to the teachings of paragraph [0005], which states the library of compounds that the present invention has developed can act cytostatically and, paragraphs [0072] and [0073] and FIGS. 1A-1 F, which teach that mibefradil blocked the calcium entry from the extracellular medium that is necessary for cancer cell division and proliferation.
First, the MPEP explicitly states that the question of compliance with the enablement requirement of 35 U.S.C. 112 first paragraph, "does not turn on whether an example is disclosed. An example may be 'working' or 'prophetic.'" The MPEP further explains that a working example can be based upon work performed, whereas a prophetic example describes an embodiment based on predicted results rather that the results actually obtained. All that is required is that there must be a correlation between the example contained in the specification and the claim. In fact, the Federal Circuit has reversed PTO decisions based on the erroneous finding that in vitro data did not support in vivo applications.
Second, the MPEP explicitly states that because "the initial burden is on the examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an in vitro or in vivo animal model." The Office Action states that "the claims are drawn to a method for inducing cytostasis comprising administering to a patient in need thereof a therapeutically effective amount of mibefradil so as to induce cytostasis in said patient; however, the specification has only presented data showing that mibefradil inhibits proliferation of prostate cancer cell lines in vitro." As such, Applicants respectfully assert that the instant 35 U.S.C. § 112, first paragraph rejection is improper because the Office Action has failed to give reasons for a conclusion of lack of correlation between the in vitro data and an in vivo.
Finally, the MPEP states that a specification need not contain a working example if the invention is disclosed in a manner such that one skilled in the art will be able to practice it without an undue amount of experimentation. It is well settled law that at times, even when the amount of experimentation required to practice the scope of the claimed invention might have been extensive, the experimentation is still routine if the necessary techniques are well known to those skilled in the art. In the specific instance of mibefradil, it is well known in the art thatcertain doses are recommended for administration to a patient in need thereof, As such, the Applicants respectfully assert that although one of skill in the art in possession of the present disclosure may need to perform routine experimentation to obtain the appropriate dose of mibefradil for therapeutic effect in a patient, such routine experimentation is not extensive, and does not rise to the level of impermissible undue experimentation.
Claims 8 and 9 are dependent upon claim 7. Accordingly, claims 8 and 9 incorporate the limitations of claim 7. As such Applicants respectfully submit that the features of claims 7-9 are enabled and comply with 112(1). Thus, Applicants respectfully request withdrawal of this rejection.

Applicant's arguments have been considered, but have not been found persuasive because as set forth above and previously set forth in the Office Action on 07/27/2011, Bertolesi et al. provides evidences that mibefradil inhibits cell growth via cytotoxic mechanisms. See title, abstract, page 214. It is noted that the specification does not show that the inhibition of cell proliferation observed is cytostatic not cytotoxic. The doses at which Applicants observe any effect, greater than 10 microM, is at least 10 times the dose Bertolesi et al. shows to be cytotoxic. See Fig. 1 of instant app. and Fig. 4 of Bertolesi et al. Thus, one of skill in the art would not be able to make and use the method as claimed to induce cytostasis in cells or in a patient with mibefradil.

Continuation of 12: The information disclosure statement filed 09/30/2011 fails to comply with 37 CFR 1.97(d) because it lacks a statement as specified in 37 CFR 1.97(e). It has been placed in the application file, but the information referred to therein has not been considered.